REMARKS

Claims

Claims 6–21 and 23 are pending of which claims 16, 12–15, 17 and 23 are currently under examination pursuant to the restriction/election requirement mailed June 20, 2007.

Claims 7–11, 16 and 18–21 are withdrawn from consideration pursuant to the aforementioned restriction/election requirement.

Claims 1–5 and 22 are cancelled without prejudice or disclaimer.

The allowability of claim 23 is hereby acknowledged.

Claim amendments

Claim 6 has been amended to conform to the USPTO's written description guidelines. See *infra* for a discussion thereof. Claims 9–21 and 23 are either directly or indirectly dependent thereon.

Claim 12 recites the fold variants of the claimed polypeptide molecule(s). Support for the amendment can be found, at least, in the disclosure contained in the Examples.

Applicants respectfully submit that the amendments presented herein do not raise new matter. Entry thereof is earnestly solicited.

Rejoinder

Withdrawn claims 9–11 along with claims 16, 18, and 20 are drawn to a method of making/using the compound(s) and/or composition(s) of the instant invention and recite all the elements of Applicants' product claims. "If a product claim is found allowable, process claims that depend from or otherwise require all the limitations of the patentable product may be rejoined." See M.P.E.P. § 806.05.

Rejoinder thereof is therefore respectfully requested.

Rejection under 35 U.S.C. §112, ¶1

Reconsideration of the rejection of claims 6, 12–15 and 17 under this section is respectfully requested.

Written description rejection

In the paragraph bridging pages 6 and 7 of the outstanding Office Action, the Examiner concedes that "Applicant is in possession of polypeptide of SEQ ID NO: 2, with a His-tag and LM and HM fold variants of SEQ ID NO: 2." She then proceeds to contend that the specification does not provide adequate written description of polypeptides *comprising* SEQ ID NO: 2 because the

transition phrase "opens the claimed variant to include additional amino acids." See page 8 of the Office Action. This contention is respectfully traversed.

Applicant has reviewed the PTO's new *Written Description Guidelines* and amended the claims in accordance with Example 9 at page 31 of the *Training Materials* (Rev. 1, March 25, 2008). While applicants may not agree with the agency's interpretation of the elements necessary to meet the statutory requirements of 35 U.S.C. § 112, ¶1, nonetheless, the pending claims have been amended to substantially conform to these.

The PTO's example provides a claim to a protein isolated from liver. A working example shows that the isolated protein was sequenced and determined to have the amino acid sequence shown in SEQ ID NO: 3. The isolated protein was additionally characterized as being 65 kD in molecular weight and having tumor necrosis activity. The exemplary specification states that the invention provides variants of SEQ ID NO: 3 having one or more amino acid substitutions, deletions, insertions and/or additions. No further description of the variants is provided. The specification indicates that procedures for making proteins with amino acid substitutions, deletions, insertions and/or additions are routine in the art. The specification does not define when a protein ceases to be a variant of SEQ ID NO: 3.

Representative Claim 1 (Analogous to instant claim 6). An isolated protein *comprising* the amino acid sequence shown in SEQ ID NO: 3.

The USPTO's own published guideline explicitly states that claim 1 satisfies the requirements set forth under §112, ¶1.

In the analytical section, it is further stated that "[although] the [exemplary] specification does not describe other members of the genus by complete structure…given the **existing knowledge in the art concerning fusion proteins, which are an example of additions that could be made to SEQ ID NO: 3**, those of skill in the art would conclude that the applicant **would have been in possession of the claimed genus at the time of filing** (emphasis added)." The same is respectfully requested.

With respect to the fold-forms of the Phl p 1 polypeptide(s) claimed herein, Applicants respectfully disagree with the PTO's contentions. However, in order to facilitate prosecution, claim 12 has been amended to explicitly recite the HM and LM fold variants. No agreement is to be implied. In view of the Examiner's statements in the last paragraph of page 6, it is submitted that the written description rejection of claims 12–14 is moot and should be withdrawn. Moreover, the disclosure contained in Figures 1–3 and the description thereof at page 5 of the originally-filed

specification provides explicit support for the claimed fold forms of SEQ ID NO: 2. Withdrawal of the rejection is respectfully requested.

Thus, it is evident that the originally-filed specification clearly provides the information set forth by the U.S. Patent Office as needed to meet the statutory requirements under §112, ¶1.

Enablement rejection

(a) Claims directed to polypeptide molecules and fold variants thereof

Based on the Examiner's statement in the paragraphs bridging pages 3 and 4 of the Office Action, further in view of the forgoing amendments, it is submitted that the alleged lack of enablement, at least with respect to SEQ ID NO: 2, his-tagged SEQ ID NO: 2, and HM/LM fold variants of SEQ ID NO: 2, is moot. Applicants' claims are directed to polypeptide molecules comprising specific sequences and chimeras thereof. Fold forms of the claimed molecules, comprising, for example, the HM and LM fold forms, are further disclosed. The detailed disclosure contained in Applicants' specification (as substantiated by the disclosure his-tagged proteins and fold forms of SEQ ID NO: 2) provides more than an enabling disclosure of how to make and use the claimed molecules. See also, the sequence listing page and the tables. The biological activities of such polypeptide molecules, for example, with respect to their reactivity to IgE molecules, are further disclosed. See, the disclosure in Fig. 3 and the description thereof at page 17 of the present application. As such, the PTO's contentions are without scientific merit.

(b) Claims directed to the pharmaceutical composition/vaccines

In the paragraph bridging pages 3 and 4, the Office Action alleges that the pharmaceutical compositions and/or vaccines of the present invention are non-enabled. This contention is respectfully traversed.

At the outset, Applicants courteously submit that the Office Action fails to present any evidence which suggests the vaccines and/or pharmaceutical compositions, as claimed herein, are not enabled. In the absence of such evidence, the rejection is deficient under controlling case law.

The burden is upon the Patent and Trademark Office to provide evidence shedding doubt that the invention can not be made and used as stated; see for example, *In re Marzocchi*, 439, F. 2d 220, 169 USPQ 367 (CCPA 1971). Moreover, Applicants' specification teaches that molecules of the present invention are useful formulation of vaccines and/or pharmaceutical compositions. See the generic teachings offered in the paragraph bridging page 12 and 13 of the present application.

In relation to a disclosure on the utilization of Phl p 1 variant polypeptides as pharmaceutical compositions, the Examiner is courteously invited to review the disclosure contained in the

Examples of the present application. See, for example, Example 2 beginning at page 17 of the instant specification, as originally filed. In this regard, Applicants' specification expressly teaches that the claimed cysteine-containing variants of Phl p1, which exhibit a different IgE reactivity profile compared to the natural allergen (nPhl p 1), can be utilized as pharmaceutical compositions or vaccines. Rationale for the use of the molecules of the instant invention in the desensitization of a subject suffering from allergy is also provided. Moreover, the disclosure in Examples and the reference cited therein (Suck et al., *International Archives of Allergy and Immunology*, 2000) expressly teach that hypoallergenic peptide molecules, such as the Phl p 1 variant polypeptide of the present invention, are useful for therapy of allergic diseases. The enclosed article by Suck et al. further establishes that the utility of allergens in vaccines and pharmaceutical compositions was appreciated by one of ordinary skilled in the art well before the filing date of the instant application. See the entire "Immunological Properties of Folding Variants" section at page 288 and the discussion section at page 289 of the enclosed Suck et al. article. Accordingly, contrary to the PTO's allegations, it is clear that the instantly claimed grass pollen allegens could be routinely manipulated and utilized as pharmaceutical preparations and/or vaccines in a manner recited in the claims.

In the penultimate sentence in the 1st paragraph at page 5 of the Office Action, it is alleged that undue experimentation would be required "to practice the claimed invention commensurate with the scope of the claims." These allegations, however, do not present any evidence to doubt the objective enablement of Applicants' disclosure. As clearly and succinctly stated by the court in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

> As a matter of Patent Office practice, then a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must** be taken in compliance with the enabling requirement of the first paragraph of §112, **unless** there is reason to doubt the objective truth of statements contained therein relied on for enabling support. (emphasis in original)

Furthermore, as stated in *Marzocchi*, at 370, the PTO must have adequate support (evidence or reasoning) for its challenge to the credibility of Appellants' statements of enablement. Thus, in the absence of evidence which demonstrates otherwise, the claims must be taken to satisfy the requirements of 35 U.S.C. § 112, ¶1.

Working examples are not required to establish enablement. As stated by the court *Marzocchi*, at page 369:

> The first paragraph of §112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.

The assertion of undue experimentation in the rejection is merely conclusory. Further, as discussed above, the specification provides more than sufficient guidance to make and use the claimed vaccines and/or pharmaceutical compositions using no more than routine experimentation. Finally, a high level of skill does not establish that one skilled in the art would have reasons to doubt the veracity of the statements in Applicants' specification with respect to the use of the claimed composition in the diagnosis, treatment, and/or prevention of the claimed conditions.

Based on the aforementioned remarks and arguments, it is respectfully submitted that Applicants' specification provides an enabling disclosure of what is claimed by the present invention. Withdrawal of the rejection under 35 U.S.C. §112, ¶1, is respectfully requested.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

No fees are believed to be due with this response; however, the Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

/Sagun KC/

Sagun KC, L0510
For Applicant(s)

/Anthony J. Zelano/

Anthony J. Zelano, Reg. No. 27,969
Attorney/Agent for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: MERCK-2975

Date: September 14, 2009